

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Art Unit	: 1635	Customer No.:	035811
Examiner	: Jane J. Zara		
Serial No.	: 10/535,692		
Filed	: May 19, 2005		
Inventors	: Annick Harel-Bellan	Docket No.:	BDM-05-1130
	: Lauriane Fritsch		
	: Redha Sekhri	Confirmation No.:	9223
Title	: METHOD FOR EXPRESSING INDUCIBLE		
	: RNAI IN CELLS, NUCLEIC ACID		
	: MOLECULES THEREFOR AND CELLS		
	: TRANSFORMED BY SAID MOLECULES		
		Dated:	December 1, 2008

RESPONSE

Mail Stop AF
Commissioner for Patents
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Sir:

This is in response to the Official Action dated August 1, 2008.

Claims 17, 19, 21-24 and 26-29 are pending. The Applicants wish to thank the Examiner for withdrawing the previous rejections under 35 USC §§102 and 112.

Claims 17, 19, 21-24 and 26-29 are rejected as obvious under 35 USC §103(a) over the combination of US '077 and US '646.

Claims 17, 19, 21-24 and 26-29 are not obvious under 35 USC §103(a) over the combination of US '077 and US '646. Reasons are set forth below.

First, the combination of US '077 and US '646 fails to teach all the elements of the claimed compositions and methods. As recited in independent Claim 1, the claimed compositions are nucleic acid molecules comprising sense and antisense sequences of RNAi placed under the control of a single transcription promoter, the sense and antisense sequences being separated by an intervening DNA sequence comprising a transcription stop site and a gene encoding an antibiotic resistance marker, wherein the intervening DNA sequence is framed at each end by a lox site. As recited in independent Claim 21, the claimed methods of transcribing RNAi in cells comprise the steps of:

- a) providing eukaryotic cells and at least one molecule of the nucleic acid described above;

- b) introducing into the eukaryotic cells the at least one molecule of the nucleic acid; and
- c) providing Cre to the eukaryotic cells such that Cre is placed in contact with the lox sites and produces site-specific recombination elimination of the intervening DNA sequence so that the sense and antisense sequences are only separated by the remaining lox sequences; whereby a single RNAi comprising the sense sequence, the lox sequence, and the antisense sequence is transcribed.

However, the claimed compositions and methods differ from US '077 and US '646 in that the intervening DNA sequence comprises a gene encoding an antibiotic resistance marker which has been specifically positioned in an intervening DNA sequence located between two loxP sites.

US '077 fails to teach all the elements of the claims. US '077 does not teach a nucleic acid configuration in which an antibiotic resistance marker is inserted in an intervening DNA sequence separating a sense and antisense sequence of RNAi. Instead, US '077 merely describes at paragraph [0118] and Fig. 28 a RNAi comprising a nucleic acid molecule in which the sense and antisense sequences of the RNAi are separated by a linker containing a transcriptional stop sequence (5'-TTTTT-3') flanked by loxP sites. Furthermore, US '077 does not provide nucleic acid compositions that achieve the advantages described below.

US '646 also fails to teach all the elements of the claims. US '646 does not teach a nucleic acid configuration in which an antibiotic resistance marker is inserted in an intervening DNA sequence separating a sense and antisense sequence of RNAi. Instead, US '646 merely discusses that an antibiotic resistance gene can be inserted in plasmids or other expression vectors to enhance the selection of the cells containing the resistance gene. Importantly, in US '646, the antibiotic resistance gene is apparently not inserted in an intervening DNA sequence located between two lox sites and, instead, appears to be a discrete transcriptional unit located in an expression vector backbone. Furthermore, US '646 does not provide nucleic acid compositions that achieve the advantages described below.

Second, one of ordinary skill in the art would not be motivated to combine US '077 and US '646 to achieve the claimed compositions and methods. The rejection states that "[t]o place the marker within the intervening sequence between the sense and antisense sequences...would be the

result of a design choice[.]” However, the rejection fails to provide a rationale as to why a person of ordinary skill would be motivated to make this one specific “design choice” based on the combination of US ‘077 and US ‘646 or given that there is a huge spectrum of other possible alternative “design choices” available.

Third, the claimed compositions and methods provide several important advantages. These advantages include:

- a) permitting the expression of double-stranded RNA in a stable manner in cells and achievement of long-term RNAi mediated effects;
- b) the ability to confirm that a nucleic acid molecule comprising the RNAi to be transcribed are in present in a cell;
- c) the ability to confirm that the RNAi to be transcribed from a nucleic acid molecule is intact; and
- d) inducing transcription of RNAi via the Cre-lox system at a specific time.

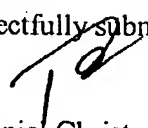
The foregoing advantages provide objective evidence of the non-obviousness of the claimed compositions and methods relative to the cited prior art.

The above discussion makes it clear that neither US ‘077 nor US ‘646 teach all the elements of the claims, that one of ordinary skill in the art would not be motivated to combine the cited references to achieve the claimed compositions or methods, and that the objective evidence indicates the claimed compositions or methods are non-obvious. Consequently, the claims are not obvious under 35 USC §103(a) over the combination of US ‘077 and US ‘646.

The Applicants respectfully request withdrawal of the rejections of Claims 17, 19, 21-24 and 26-29.

In light of the foregoing, the Applicants respectfully request that the entire application is now in condition for allowance, which is respectfully requested.

Respectfully submitted,


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